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Title

Association of snus experimentation in late adolescence with daily cigarette smoking in early adulthood: A longitudinal study among Finnish men

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Keywords

Snus, moist snuff, smokeless tobacco, smoking initiation, daily smoking

ABSTRACT

Aims: Swedish smokeless tobacco (snus) is a lower-risk tobacco product than is cigarette smoking for individuals. However, the public health impact of snus use is less well studied. Critically, uncertain is whether use of snus leads to onset of smoking. This study aimed to investigate prospectively the association between snus experimentation in late adolescence and daily cigarette smoking in early adulthood among Finnish young men.

Methods: Data were obtained from 1090 young men within the population-based FinnTwin12 cohort. At baseline (mean age 17 years), we assessed lifetime use of cigarettes and snus, plus other potential predictors of cigarette smoking. At follow-up (mean age 24 years), participants were categorized according to their current smoking status. The final analyses were conducted among 375 young men who were never smokers at baseline with adequate data on follow-up smoking status and other potential predictors of cigarette smoking.

Results: Age-adjusted logistic regressions showed an increased risk of becoming a daily smoker at follow-up among those participants who had at least tried snus but had never smoked cigarettes at baseline (OR 6.48, 95% CI 2.02-20.7), compared with those who had never used snus. When additionally adjusted for monthly alcohol intoxication, maternal smoking, and peer drug use, the association between snus experimentation and later daily cigarette smoking was attenuated, but remained significant (OR 3.94, 95% CI 1.22-12.7).

Conclusions: Our data provide suggestive support for the proposition that snus experimentation during late adolescence is longitudinally associated with daily cigarette smoking in early adulthood. Although a causal association cannot be inferred with certainty, snus experimentation might constitute an indicator of propensity to proceed to regular snus use and initiation of use of other tobacco or nicotine products.

BACKGROUND

Snus, or Swedish-type moist snuff, is a smokeless tobacco product. Snus is available in loose form and small porous bags, which are placed between the upper lip and gingiva for about one hour, leading to nicotine intake [1]. Nicotine absorption from snus is slow, but reaches higher and more prolonged plasma levels in venous blood than do cigarettes [2]. Snus is low in tobacco-specific nitrosamines, a group of carcinogenic compounds found in tobacco products [3]. Epidemiological data suggest that the adverse health consequences of exclusive snus use are smaller than those of cigarette smoking, and that the incidence of major health outcomes studied so far does not differ between exclusive snus users and non-users of tobacco [4, 5]. However, in many cases the evidence is not conclusive, and the SCENIHR (Scientific Committee on Emerging and Newly-Identified Health Risks) continues to regard snus, along with other smokeless tobacco products, as hazardous to health [6].

Due to its potential adverse health effects, snus sales are banned in the European Union with the exception of Sweden, a country with a long history and high prevalence of snus use [7, 8]. Outside the European Union, there is a well-established market for snus in Norway [9], and this product was introduced onto the USA market in 2006, yet with low acceptance [10]. In Finland, the ban on snus sales adopted in 1995 has not prevented individuals from obtaining snus through friends, personal imports, and under-the-counter sources [11]. On the contrary, snus use among Finnish adolescents has increased after the ban [11]. School surveys in Finland show that 27% of Finnish boys have tried snus, while 13% use snus currently and 3% are daily users [12]. According to recent national surveys in the Finnish adult population, current snus use is also common among young men: 4.8% use snus daily and 6.8% occasionally in the age group of 15 to 24 years, while in the group of 25 to 34 years 5.2% use snus daily and 8.1% occasionally[13]. Women report snus use much less frequently [12, 13].

Because of its addictive nature and increasing use among young populations, concern has emerged regarding a potential association between the use of smokeless tobacco products and later cigarette smoking [14]. While some evidence supports this hypothesis [15, 16], others studies do not support it [17, 18]. In the case of snus, longitudinal studies investigating this association among adolescents have found mixed results in diverse cultural settings [19-23]. A review on studies investigating the association between use of snus and later cigarette smoking reported that research designs in this field have been often inadequate [24]. The main methodological problems include lack of adjustment for confounders, dissimilar time available for smoking initiation between different groups, use of unrepresentative small samples, and lack of accounting for previous exposure to cigarette smoking at baseline [24]. A comprehensive list of potential predictors of smoking initiation among adolescents should include data on parental and peer smoking, use of alcohol and illicit drugs, and family structure [25, 26]. Such potential confounders have not been addressed simultaneously in earlier studies. Thus, interpretation and comparability of these results is limited, and the research question remains unanswered.

In view of the current worldwide tobacco epidemic and the large consequences of cigarette smoking on human health, there is need for preventive strategies to keep adolescents and young adults from initiating use of cigarettes [27]. Some researchers have suggested that lifting the ban on snus sales in the European Union would have a positive public health impact by discouraging smoking initiation and by helping inveterate smokers to quit cigarettes [28, 29]. On the other hand, making this product more easily available could have negative public health consequences if snus use is shown to increase the likelihood for smoking initiation among individuals who would have otherwise stayed tobacco-free [23].

AIM

This study aimed to investigate prospectively the association between snus experimentation in late adolescence and daily cigarette smoking in early adulthood among Finnish young men.

METHODS

Data

Data were obtained from the FinnTwin12 study for which detailed information on the sample and assessment waves has been published earlier [30-32]. Briefly, in FinnTwin12, 5600 Finnish twins born 1983 through 1987 were sequentially enrolled and four waves of data have been collected so far, at mean ages 12, 14, 17 and 24. Response rates were high in the first three waves (87-92%), and slightly lower in the fourth one (80%). We used information from the third and fourth waves, with data collection taking place in 2000-2005 and 2006-2011, respectively. Additional data were obtained from questionnaires filled by the participants' parents when the twins were 12 years old. Maternal and paternal response rates were 85% and 77%, respectively.

The third wave questionnaire at mean age 17, the baseline assessment for our analysis, inquired whether the twins had smoked at least one cigarette at that stage in their lives. Lifetime use of snus was assessed as follows: never, once, two to 50 times, over 50 times, and regular use. Lifetime use of illicit drugs was similarly investigated as follows: never, one to three times, four to nine times, ten to 19 times, and over 20 times. Questions regarding alcohol use inquired about frequency of drinking and of intoxicating, with response options ranging from never to daily. Peer cigarette smoking and lifetime use of illicit drugs were asked as follows: no, one, two to five, and over five peers. In addition to their siblings, family structure options included: mother and father, mother and stepfather, father and stepmother, only mother, only father, others. When the twins were aged 12, their parents were asked in

maternal and paternal questionnaires whether they had smoked over 5 packs (100 cigarettes) during their lifetime, and whether anyone smoked inside their homes at the time of the survey. At follow-up, young adult twins were asked about their current smoking status, ranging from never to daily cigarette smoking.

Variables

Our aim was to assess the association between snus experimentation and later cigarette smoking among young adult men. In our full sample (n=1090), lifetime snus use at baseline was 34.9% (12.8% had tried once, 16.6% two to fifty times, 3.67% over fifty times and 1.74% used regularly). Among the restricted sample, i.e. never smokers at baseline (n=375), lifetime snus use was 4.8% (3.2% had tried once, 0.8% two to fifty times, 0.3% over fifty times and 0.5% used regularly). Because subcategories of snus users among men who had never smoked at baseline contained only a few individuals, we decided to dichotomize snus use as 'any use' vs. 'never use' in order to increase the statistical power of the group exposed to snus.

In order to assess both the independent and cumulative effect of potential predictors of cigarette smoking by performing crude and multiple adjusted logistic regression analyses, we also dichotomized other variables, as follows: lifetime ever cigarette smoker of at least one cigarette (yes/no), lifetime ever user of illicit drugs (yes/no), alcohol user (yes/no), monthly alcohol intoxication (yes/no). Peer smoking and ever use of illicit drugs were considered to be present if the twin reported to have at least one peer who was using or had used these substances, respectively. Intact family structure was dichotomized as currently living with both biological parents (yes/no). Parental smoking was defined as never vs. ever smoker for each parent. Smoking inside home when the twins were aged 12 was dichotomized as no-one smoking inside home vs. someone smoking inside home, combining responses from both

parents. We also considered type of schooling at age 17, when the twins themselves reported their current student status. The responses for this item in our survey were classified into three groups: (1) not studying currently, (2) in vocational school, (3) in academically oriented upper secondary school. We scored the three responses dichotomously (0=academically oriented school, 1= vocational school or not studying).

The outcome variable was daily smoking at the time of the follow-up (mean age 24 years). The initial question to assess smoking status was as follows: "Which of the following best describes your present smoking habits?" and the options were as follows: 1) I smoke daily 20 cigarettes or more; 2) I smoke daily 10-19 cigarettes; 3) I smoke daily 5-9 cigarettes; 4) I smoke daily 1-4 cigarettes; 5) I smoke once a week or more often but not daily; 6) I smoke less often than once a week; 7) I am trying to quit or have quit smoking; 8) I have tried smoking but I do not smoke now; 9) I have never smoked. Responses were scored to dichotomize individuals at follow-up based on self-reports of current daily smoking (yes/no), the former including daily smokers (options 1-4) and the latter including non-daily smokers, quitters and never smokers (options 5-9).

Statistical analyses

We used logistic regression analyses to estimate the odds ratio (OR) and 95% Confidence Intervals (CI) of being a daily smoker at follow-up given any baseline exposure to snus and other potential predictors of daily smoking at follow-up. Other potential predictors were chosen based on literature and their associations with the outcome were tested in the age-adjusted analyses. Those predictors which were significant in these age-adjusted analyses were then included in the multiple adjusted model. Thus, the association of snus use with later daily cigarette smoking was simultaneously adjusted for those other predictors. We analysed the twins as individuals. Because the twins were sampled as clusters, the primary sampling

unit being the twin pair, the clustering of correlated observations from twin pairs was controlled for when computing standard errors of the estimates using robust estimators of variance. Similarly, the survey design option was used when estimating p-values in the chi-square test [33]. We also compared characteristics between those participants who answered all relevant questions (i.e. valid analysis sample) and those participants with missing values in them. The Stata 13.1 software version was used.

RESULTS

Sample characteristics

From the 5600 twins originally enrolled in this cohort, 4236 (75.6%) responded at age 17. Among them, 3402 (80.3%) provided a response as young adults. Of those who responded to both surveys, 2557 (75%) provided information for all variables included in our analysis. Of them, 1090 (42.6%) were men with age ranging from 17.2 to 18.2 (mean 17.6, SD 0.20) at baseline, and from 20.9 to 27.5 (mean 24.1, SD 1.68) at follow-up. Although response rates in each assessment were high, the decrease in the number of participants reflects dropouts over several surveys. Furthermore, some participants did not answer all questions included in our analyses and were therefore excluded. Compared with those having complete data, the participants with missing information were significantly ($p<.05$) more often ever smokers of at least a single cigarette (74% vs. 68.2%), ever snus users (32.4% vs. 22.3%), ever users of illicit drugs (15.5% vs. 12.1%), and with higher rates of monthly alcohol intoxication (40% vs. 34.1%). In addition, they were more often not living with both biological parents (35.7% vs. 16.4%), and were more likely to have smoking fathers and mothers (69.0% vs. 65.3% and 58.1% vs. 50.2%), who were also smoking inside their homes to a higher extent (11.6% vs. 8.13%). Daily smoking at follow-up was higher among those who provided data on their

smoking status at follow-up but had missing information in other variables assessed, compared with those who provided information in all domains (30.7% vs. 23.7%).

Table 1 shows characteristics of 1090 men, including also baseline ever smokers. By the mean age of 17 years over 60% had ever at least experimented cigarette smoking whereas around 35% had ever used snus. At the mean age of 24 years, about 26% reported being daily smokers. At baseline 34.9% (n=380) had used snus at least once (12.8% once, 16.6% 2-50 times, 3.67% >50 times, 1.74% used regularly).

Snus use and other predictors of daily cigarette smoking

Among all baseline snus ever users 43.7% (n=166) were daily smokers at follow-up, whereas among never snus users only 16.1% (n=114). However, among the baseline never smokers with non-missing data on relevant variables (n=375), altogether 6.67% (n=25), out of which 27.8% (n=5) of snus users and 5.60% (n=20) of never snus users, became daily smokers at follow-up (table 2).

Age adjusted logistic regression analyses were performed for potential predictors of daily cigarette smoking at follow-up among men who were never smokers at baseline. Those participants who had at least tried snus but had never smoked a cigarette at baseline had about six-fold likelihood (OR 6.48, 95% CI 2.02-20.7) for daily cigarette smoking, compared with those who reported no snus use at baseline. Other significant predictors of daily cigarette smoking included monthly alcohol intoxication, peer use of illicit drugs and maternal smoking (table 2).

Table 3 shows the results of two multiple logistic regression analyses, adjusted for age and for other predictors of daily cigarette smoking that were significant in the age adjusted analyses among those who were never smokers at baseline. The final adjusted model included all four variables (lifetime snus use, monthly alcohol intoxication, maternal smoking and peer use of

illicit drugs) in addition to age. The association between snus experimentation and later daily cigarette smoking was attenuated, but remained significant (OR 3.94, 95% CI 1.22-12.7). Further, we conducted a sensitivity analysis where we excluded those who reported to be 'quitters' at follow-up (n=9). In the adjusted model the association of snus experimentation with daily smoking remained similar (OR=3.88, 95%CI 1.21, 12.5).

DISCUSSION

Snus experimentation during late adolescence predicted becoming a daily smoker in early adulthood among men who were never smokers at baseline. The six-fold odds ratio was attenuated to four-fold likelihood but remained significant after including other significant predictors of daily cigarette smoking, such as alcohol intoxication and maternal smoking. The rapid transition from non-existent smoking to daily cigarette smoking in just a few years suggests a quick development of nicotine dependence [34], which could be partially explained by the use of smokeless tobacco products, such as snus [35].

Prior longitudinal studies on this subject have produced conflicting results. Among Swedish adolescents, exclusive snus use predicted tobacco use but did not predict cigarette smoking [19]. Similar results were found among Norwegian adolescents: exclusive snus use in early adolescence was associated with dual use in late adolescence but not with exclusive smoking [20]. In Finland, a study among 2816 students followed from age 13 to 16 showed that snus experimentation among male adolescents predicted later weekly smoking [21]. As found in our study, snus experimentation at baseline was rare among Finnish girls [21]. A recent study among 1696 young adults in the USA followed from 2010 to 2012 found an increased risk for current smoking at follow-up among non-smokers at baseline who had tried snus [22]. Nevertheless, the definition of non-smoker at baseline was restricted to 30 days before the survey and therefore did not account for previous exposure to cigarette smoking [22]. Another

longitudinal study among adolescents and young adults in the USA who had never smoked cigarettes at baseline concluded that snus experimentation predicted cigarette initiation, current cigarette smoking and smoking intensity [23]. Most of these prior studies lacked adjustment for well-known predictors of smoking initiation, such as parental smoking, family structure and alcohol use.

Late adolescence may not be the most sensitive period to study factors predicting smoking initiation, since a high percentage of the population has been exposed to cigarette smoking by this age [36]. However, our results confirm the existence of a group of individuals in this stage who remain susceptible to start smoking and therefore remain as an important target for preventive interventions [37]. Although peer smoking has been pointed out as one of the strongest predictors of regular cigarette smoking among adolescents [38], our results suggest that peer smoking during late adolescence no longer is predictive of smoking initiation in early adulthood, probably because those individuals who are more susceptible to social influences have already experimented with cigarettes by this age. Interestingly, type of school track (academic, vocational, not attending school) reported at age 17 was not a significant predictor of later daily smoking in our data set, which was restricted to never smokers at baseline. On the other hand, and consistent with previous studies [39], maternal smoking remained as a significant predictor of daily cigarette smoking in our sample, an effect that can be explained by both environmental and genetic factors [40]. Monthly alcohol intoxication also predicted daily cigarette smoking. This was expected, as smoking and alcohol abuse tend to converge in a cluster of unhealthy behaviours [41].

In addition to the potential association between snus use and cigarette smoking initiation, dual use of snus and cigarettes has emerged as a matter of concern in Finland as snus has become more popular in this country, especially among young males [42]. As use of smokeless tobacco products is not affected by anti-smoking regulations, such as smoking bans in public

places and restaurants, individuals with high nicotine dependence can switch from one product to another depending on the circumstances, maintaining their addiction [43]. In social terms, dual users have been described as a high risk group compared with exclusive snus users, exclusive smokers, and non-users of tobacco, showing larger social disadvantage and unhealthy lifestyles in adulthood [44], as well as a less favourable profile of risk vs. protective factors in adolescence [45].

Rather than a gateway effect between snus use and cigarette smoking initiation our results suggest that, in line with another Finnish study [46], snus experimentation may be part of a cluster of risky behaviours that might predispose individuals to take up daily smoking even at ages where smoking initiation is less common. Furthermore, we would like to acknowledge the evidence provided by a meta-analysis, where the use of e-cigarettes in adolescence predicted cigarette smoking in adulthood [47] and by a recent study, where any use of e-cigarettes, hookah, non-cigarette combustible tobacco, or smokeless tobacco was independently associated with later cigarette smoking [48].

Strengths and limitations

Our longitudinal study, performed in a large and representative sample of Finnish adolescents followed-up until young adulthood has the advantage of minimizing recall bias by establishing a clear temporal relationship between order of use of products and other variables. Our final model includes adjustment for a comprehensive set of potential confounders, which enriches the robustness of our conclusions. Because participants who were excluded from the analyses due to missing information were more often lifetime snus users at baseline, and daily smokers at follow-up, we could be underestimating the strength of this association because of these selective exclusions.

Regarding the main limitations of our study, the large confidence intervals found are explained by the low exposure to some of the explanatory variables among never smokers, as some of the cells contained only a few individuals. In the case of snus experimentation, never smokers who transitioned to daily smoking at follow-up had tried snus once or twice at baseline, which limits the explanatory power of this variable regarding potential further implications of snus experimentation. Thus, because of those wide confidence intervals, our results should be interpreted with caution. The association between snus experimentation and cigarette smoking was attenuated when adding covariates in the model, with the possibility of residual confounding via other psychosocial variables, such as school performance and attitudes towards cigarette smoking, not adjusted for in our study [49].

We acknowledge that logistic regression analysis is not the most optimal method for this kind of study because it does not account for the time at when the event (i.e. initiation of daily smoking) occurs. Unfortunately, our data do not include the date of the event and therefore we chose to apply logistic regression. We also acknowledge that our outcome was relatively rare, i.e. there were only 25 daily smoking men at follow up among the baseline never smokers, and hence we have relatively wide confidence intervals for our estimates.

CONCLUSIONS

Our results provide suggestive support for the proposition that snus experimentation during late adolescence is longitudinally associated with daily cigarette smoking in early adulthood, even when other predictors of cigarette smoking are accounted for. It seems unlikely that a single-time use of snus could explain by itself a habit that emerges years after the exposure to this product; thus, a causal association between early snus use and later cigarette use cannot be inferred with certainty. However, snus experimentation might constitute an indicator of

propensity to proceed to regular snus use and to initiate use of other tobacco or nicotine containing products.

CONTRIBUTORS

DA, TK, TL, and JK conceptualized the research questions. DA conducted all analyses, prepared tables and drafted the manuscript. DA, TK, TL, AH, RJR, and JK contributed to the interpretation of findings, identification of the implications and critically revised the manuscript.

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COMPETING INTERESTS

Tellervo Korhonen and Jaakko Kaprio have consulted for Pfizer on nicotine dependence between 2011 and 2016. Other authors declare no competing interests.

ETHICS APPROVAL

Ethical permission for the FinnTwinT12 study was obtained from the University of Helsinki, the Helsinki and Uusimaa Hospital district ethical committee, and the Institutional Review Board of Indiana University.

DATA SHARING STATEMENT

Twins are easily identifiable and therefore data is not shared, but researchers are invited to contact the authors regarding additional analyses.

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Table 1. Characteristics of the full sample (n=1090 men)

Variable	N (%)
Baseline variables (mean age 17.6)	
Lifetime cigarette experimentation	715 (65.6)
Lifetime snus use	380 (34.9)
Lifetime use of illicit drugs	113 (10.4)
Alcohol drinking	936 (85.9)
Monthly alcohol intoxication	400 (36.7)
Not living with both biological parents	184 (16.9)
Vocational school or not studying	433 (39.7)
Peer cigarette smoking	964 (88.4)
Peer lifetime use of illicit drugs	582 (53.4)
Parental variables	
Maternal lifetime ever smoking (over 100 cigarettes)	554 (50.8)
Paternal lifetime ever smoking (over 100 cigarettes)	718 (65.9)
Someone smoking inside home	96 (8.81)
Follow-up variable (mean age 24.1 years)	
Current daily smoking	280 (25.7)

Table 2. Logistic regression analyses[a] on potential predictors of daily cigarette smoking at follow-up among men who were never smokers at baseline (n=375)[b]

Potential predictors of daily smoking	Daily smoker at follow-up and predictor positive	Daily smoker at follow-up and predictor negative	OR	95% CI
Lifetime snus use	27.8% (n=5/18)	5.60% (n=20/357)	6.48	2.03-20.7
Lifetime use of illicit drugs	0	6.67% (n=25/375)	-	-
Alcohol drinking	8.27% (n=22/266)	2.75% (n=3/109)		